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ABSTRACTS

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CLINICAL STUDIES, TUBERCULOSIS

Tuberculin in Bone and Joint Disease.—It is important but frequently impossible to diagnose bone and joint tuberculosis early. The tuberculin reaction is usually more reliable in these than in other forms of tuberculosis. The reaction is stronger when tuberculin is applied near the tuberculous focus than when applied in other areas. Therefore, Mantoux tests were made over the diseased bone or joint and on a symmetrical point of the body. In 88 (82.2 per cent) of 107 cases, the reaction was more strongly positive over the tuberculous focus. The method was equally reliable in fresh and in older tuberculous diseases of bones and joints; it was perhaps less reliable when foci were located from the surface, as in coxitis and spondylitis.—*Die Tuberkulinreaktion im Dienste der Differentialdiagnose bei Knochen-und Gelenkerkrankungen, E. Wiesner & R. Reiter, Wien. klin. Wchnschr., January, 1954,* ***66:*** *38.*—(*G. C. Leiner*)

Esophageal Tuberculosis.—Four cases of esophageal tuberculosis were diagnosed from 1949 to 1953. More esophageal tuberculosis is being reported in elderly patients since it has been recognized that caseous lymph nodes may perforate into the bronchus or the esophagus and so spread the disease. Except for dysphagia or signs of stenosis, symptoms are usually lacking and there is no typical radiographic picture to aid in the diagnoses. Most often esophageal tuberculosis is diagnosed at autopsy, following a biopsy to exclude malignancy, or when radiation fails to relieve a suspected carcinoma without biopsy confirmation.—*Kasuistische Beiträge zur Oesophogustuberkulose, W. Pulver & F. Michel, Schweiz. med. Wchnschr., February 13, 1954,* ***84:*** *221.*—(*E. Dunner*)

Primary Intestinal Tuberculosis.—Among 100 pulmonary tuberculous patients, 10 had mesenteric calcification, residuals from an old primary intestinal complex. Despite some exogenous superinfection, several of these patients probably had progressed from their primary abdominal infection. Primary intestinal infection seems less benign than is commonly believed.—*Tuberculose abdominale et phtisie pulmonaire, E. C. Bonard, Schweiz. Ztschr. Tuberk., January, 1954,* ***11:*** *1.*—(*E. Dunner*)

Intrathecal Streptokinase.—Streptokinase may be employed under three distinct circumstances in the therapy of tuberculous meningitis; these circumstances profoundly influence the nature of its employment and the chances of success. These uses are (*1*) prophylactically before obstruction of the cerebrospinal channels, (*2*) therapeutically for established or pending subtentorial and basal cisternal block, and (*3*) therapeutically for spinal block. A lower dosage limit may be imposed by the presence of inhibitors, so that no free fibrinolytic enzyme is produced below it. An upper limit of intrathecal dosage is also present, since high concentrations of streptokinase produce systemic upsets and local irritation of the spinal theca will result in the failure. Laboratory examination of the cerebrospinal fluid is essential to estimate the correct dose. The customary intrathecal dose of streptokinase (100 Christensen units) is usually insufficient to produce free fibrinolytic enzyme. Patients vary considerably, but the

optimal intrathecal dose usually lies between 300 to 3,000 units of streptokinase; a standard dose cannot be stated. This may explain the variable clinical results. Actually streptokinase may be used with reasonable success, either prophylactically or for the treatment of subtentorial or basal cistern block; the chances of successful treatment of spinal block by this means are small.—*Intrathecal fibrinolysis with streptokinase in tuberculous meningitis, A. P. Fletcher, J. Clin. Investigation, January, 1954, 33: 69.—(E. Dunner)*

Acute Appendicitis During Pneumoperitoneum.—During the past five years, 31 cases of acute appendicitis were observed in the presence of pneumoperitoneum. Pneumoperitoneum presents certain hazards, foremost among them the masking of acute appendicitis. Acute appendicitis appears to be more frequent among patients with pneumoperitoneum than among those receiving other antituberculous therapy. This observation cannot be satisfactorily explained. The onset of the appendicitis does not always conform to the characteristic clinical syndrome, but abdominal pain is by far the most consistent symptom. Tenderness to direct pressure is the most constant physical finding, rebound tenderness, rigidity, muscle guarding, and so forth, being conspicuously absent. When appendicitis is suspected, the intraperitoneal air should be aspirated as a preoperative as well as a diagnostic measure. Lack of peritoneal and omental response to inflammatory disease is the most common operative finding, and the diminished intraperitoneal defenses make appendicitis and peritonitis much more dangerous. It is, therefore, imperative to operate when the diagnosis is equivocal; conservatism leads to disastrous results.—*Acute appendicitis in the presence of pneumoperitoneum, T. S. Raiford & J. A. M. Thompson, Ann. Surg., January, 1954, 139: 117.—(M. J. Small)*

Pregnancy After Pulmonary Resection.—Among 14 patients who had had pulmonary resection for tuberculosis, including 10 pneumonectomies, there were 15 uncomplicated pregnancies, 15 normal deliveries, and 15 living children, all in good condition. Only one patient reactivated her tuberculosis during the sixth week of pregnancy. She had had a pneumonectomy eighteen months previously. After therapeutic abortion and streptomycin therapy, the patient improved and had an uneventful pregnancy eighteen months later. Most of the 10 patients with pneumonectomy had very serious involvement before resection; 7 had "destroyed lung." Patients with unilateral disease and an uncomplicated postoperative course, however, rarely have progression in the remaining lung after the first year. After this time interval, pregnancy usually is safe and therapeutic abortion is unjustified. All of the patients in this series tolerated pregnancy remarkably well and most continued their usual activities until the sixth month. Late in pregnancy some patients had dyspnea, but none had respiratory insufficiency or cardiac decompensation.—*Grossesse et accouchement après exérèse pulmonaire pour tuberculose, M. Bérard, G. Maret, & E. C. Santier, Rev. de la tuberc., 1953, 17: 1098.—(V. Leites)*

Partial Pulmonary Resection for Tuberculosis.—A series of 50 pulmonary resections for tuberculosis were performed between 1949 and 1951. Of the 20 patients who survived pneumonectomy, 19 are clinically, bacteriologically, and roentgenologically in good condition. Of 20 cases of partial resection, one patient died of bronchopleural fistula, and 3 others reactivated to old ipsi- or contralateral foci. Improved surgical techniques and the rational use of antibiotics have contributed to better results. In a series of 66 pneumonectomies performed since 1951, the mortality has dropped from 25.9 per cent to 21.8 per cent. For partial resections the respective figures have been 20 per cent and 2.9 per cent. With these improved results, surgery is now indicated in cases heretofore reserved for collapse therapy. Increasing

anatomopathologic and bacteriologic knowledge of the pulmonary lesions has also extended the indications for surgery to cases previously considered stable by clinical and bacteriologic criteria; residual necrotic foci should be excised.—*Resección parcial optativa en tuberculosis., J. Ramírez Gama, A Estrada S., J. L. Ochoa, & R. Montes., Rev. mex. de tuberc., July, 1953,* ***14:*** *371.—(F. Perez Pina)*

Amino Acid Supplement.—The amino acid content of the blood is the same in patients with pulmonary tuberculosis as in healthy persons. Adding amino acids to the food of seriously ill tuberculous patients influences favorably the course of otherwise refractory cases.—*Comportement et usage thérapeutique des acides aminés chez lès tuberculeux pulmonaires, G. Favez, Schweiz. Ztschr. Tuberk., February, 1954,* ***11:*** *97.—(E. Dunner)*

CLINICAL STUDIES, NONTUBERCULOUS DISEASES

Suppurative Pneumonia.—Although suppurative pneumonia is estimated to account for less than 10 per cent of all childhood pneumonias, it probably causes more deaths than other forms of inflammatory pulmonary reaction. The disease occurs chiefly by bronchogenous invasion. Several roentgenographic features are distinctive during the development of acute suppurative pneumonia. Perhaps most consistent is the rapidly changing roentgen picture. A roentgenogram of the chest may show an area of homogenous infiltration, soon followed by a large pulmonary cavity containing a fluid level and, later, a large pleural effusion or tension pneumothorax. These changes may occur while the clinical course remains constant. At times, the roentgenogram may show only mild emphysema while there is overwhelming toxicity. Another characteristic roentgenographic feature is the development of pneumatoceles, which disappear spontaneously as the infection subsides. The parenchymal changes are densities of the focal, segmental, or lobar type. Lobar densities are more frequently due to confluent atelectasis than to pure consolidation. Nontraumatic pneumothorax in an infant should immediately suggest an underlying suppurative pneumonia.—*Roentgen studies in suppurative pneumonia of infants and children, J. A. Campbell, D. C. Gastineau, & F. Velios, J.A.M.A., February 6, 1954,* ***154:*** *468.—(H. Abeles)*

Pneumonia in Infants.—The triad of pneumonia followed by pneumatocele and spontaneous pneumothorax was seen in 3 babies, six weeks, seven weeks, and five months of age, respectively. The entire process was benign, although the babies were alarmingly ill at the onset with cyanosis and dyspnea.—*Triad of pneumonia, pneumatocele, and spontaneous pneumothorax in infants, H. E. Bass, N. Diamond, & M. Schuman, J.A.M.A., January 9, 1954,* ***154:*** *143.—(H. Abeles)*

Staphylococcus Pyopneumothorax.—Among 41 pneumonopathies in children, there were 27 cases (65.8 per cent) of pyopneumothorax. Of the children, 16 were less than two years of age. Of the lesions, 33 per cent were primary and 67 per cent secondary to staphylococcic infection of the lung. The prognosis was determined by (*1*) the age of the patient; the younger the patient, the higher the mortality; (*2*) the susceptibility to antibiotics; and (*3*) the type of treatment. Treatment consisted of local and parenteral antibiotic injections. Before the susceptibility of the organism was determined, massive penicillin doses and another antibiotic, usually chloramphenicol, were begun. If fifteen to twenty days' treatment and thoracenteses did not improve the child, closed intercostal drainage was instituted. Open thoracotomy was rarely indicated. Only one patient was subjected

to decortication and none to resection, but antibiotic treatment was prolonged. The pulmonary lesion resolved slowly, but in children the ultimate radiographic clearing sometimes was so complete that it was difficult to distinguish the affected side.—*Les pyopneumothorax à staphylocoques du nourisson et de l'enfant, J. Chaptal & A. Campo, Poumon, January, 1954, 10: 49.—(F. S. Lansdown)*

Staphylococcus Pyopneumothorax.—Pyopneumothorax is always secondary to a pulmonary staphylococcic infection, whether recognized or not. The staphylococci probably enter through bronchi to produce pulmonary lesions which evolve by successive steps; the pyopneumothorax may occur at any stage. The initial staphylococcic pneumonia may kill the patient rapidly, may resolve entirely, but, most commonly, localizes as an abscess. With antibiotic therapy, the abscess may resolve, become chronic, or form bullae. These bullae may fatally compromise respiration. Pyopneumothorax, almost always the result of perforation of an abscess or a bulla, gravely threatens the patient's life, either by toxemia or by mechanical compression of the lung. Anatomically, the lesion may be (*1*) pyopneumothorax localized by adhesions, (*2*) generalized pyopneumothorax without mediastinal displacement, or (*3*) generalized pyopneumothorax with mediastinal displacement. The third is by far the worst and is most apt to afflict the newborn, whose mediastinum is extremely elastic. This probably explains why the highest fatality rate is in the youngest age group. In a series of 41 cases, 70 per cent occurred between December 31 and March 31. The patients were a few days to ten years of age, 26 being less than six months old. In 26 cases, the initial focus could be identified. It was in the upper respiratory tract of 16 patients, in the skin of 8, and in the mother, as a breast abscess or furuncle in 5. In 31 cases, the antibiotic susceptibility of the staphylococci was tested; 8 strains were susceptible to penicillin, 22 to streptomycin, 20 to chlortetracycline, 19 to oxytetracycline, 24 to chloramphenicol, and 7 to sulfonamides. Only one strain was resistant to all drugs, and 2 were susceptible only to chloramphenicol. Of the 41 patients with pyopneumothorax treated, 16 were given only conservative treatment, which included repeated needle aspirations of fluid and air, local and parenteral instillations of the appropriate drug, and general supportive measures; 11 (65 per cent) died, and 5 were cured. Other reported series had a 70 to 85 per cent mortality. None of the 7 patients with mediastinal displacement recovered. The 25 later cases were treated medically or surgically as appeared indicated. Initially, they all had conservative treatment, but this was abandoned if the mediastinum was displaced. These procedures produced 7 cures, 2 deaths, and 16 "failures." The "failures" then had intercostal drainage or thoracotomy. Among the 13 cases drained, there were 5 cures, 2 deaths, and 6 "failures." All of these "failures" were later cured by thoracotomy. Of the 9 patients who had thoracotomy, 3 had not had earlier intercostal drainage and all 9 were cured. Thus, medico-surgical management cured 84 per cent of the patients, and the following principles can be formulated: (*1*) Good medical treatment is absolutely necessary, using antibiotics in massive doses and following as rapidly as possible the indications of the susceptibility tests. (*2*) Local treatment by thoracentesis is permissible when there is no mediastinal displacement. (*3*) When mediastinal displacement occurs, conservative treatment is dangerously ineffective and immediate intercostal drainage is indicated. (*4*) Open thoracotomy to free the lung and resect residual disease is not emergency treatment but may be done, without apprehension, early if medical measures and intercostal drainage fail.—*Les pyopneumothorax à staphylocoques de l'enfant leur traitement médico-chirurgical, J. Mathey, J.-P. Binet, G. Oustrières, C. Attal, G. Vermeil, & Ch. Bach, Poumon, January, 1954, 10: 19.—(F. S. Lansdown)*

Staphylococcus Pyopneumothorax.—Lung abscess, acute pneumonia, frequently with

bullous pneumonopathy, as well as purulent pleurisy cause pyopneumothorax. The lesion may occur when a pulmonary abscess or bulla ruptures or when a purulent pleurisy perforates into the lung. Among 33 patients treated, the mortality was 52 per cent. Three patients with moderate functional impairment were all cured, one by drainage and 2 by needle aspirations. Of 20 patients who had severe respiratory symptoms, 13 were subjected to drainage and 6 (46 per cent) of these died. Of 7 not drained, 6 (85 per cent) died. Of the 6 deaths following drainage, 2 were from extrathoracic foci in the middle ear and brain, one followed a contralateral pneumothorax, 2 followed sudden progression of the respiratory symptoms when drainage was delayed, and one was from sudden mediastinal and subcutaneous emphysema. Of the 6 patients who died without drainage, one succumbed to nephritis and otitis and the other 5 to fulminating respiratory failure. All but one in this group were less than eighteen months of age. In children and infants, pyopneumothorax usually causes death through mechanical accidents. Drainage should be undertaken early, whatever the age of the child. It should be supplemented by vigorous and appropriate antibiotic treatment.—*Les pyopneumothorax à staphylocoques de l'enfant, M. Jaubert de Beaujeu & J.-C. Sournia, Poumon, January, 1954,* ***10:*** *43.—(F. S. Lansdown)*

Bronchiectasis.—Bronchiectasis presents several paradoxes. Widespread bronchial ectasia in one patient may produce few symptoms; another may have a small septic focus, occasionally without demonstrable dilation, that causes crippling symptoms. Most patients with septic bronchiectasis present no great problem in diagnosis and treatment. A smaller but significant group have long-standing and distressing symptoms of pulmonary sepsis and still offer inconclusive or misleading diagnostic evidence, both visual and clinical. The only cure of septic bronchiectasis is excision. When surgery is absolutely contraindicated, postural drainage, respite from irritants, and intelligently applied antibiotics may palliate the disease. Modern man's erect position is one of the prime factors in the establishment and maintenance of bronchiectatic sepsis.—*Paradox of bronchiectasis, R. H. Overholt, F. M. Woods, & S. W. Atwell, J.A.M.A., January 16, 1954,* ***154:*** *193.—(H. Abeles)*

Cardiac Echinococcosis.—Primary cardiac hydatidosis involving the left ventricle occurred in a 46-year-old white man who had dyspnea, marked cyanosis, engorged neck veins, edema of the legs, hepatomegaly, and ascites. Pulsus alternans was also noted. A chest roentgenogram showed a large rounded shadow in the superior mediastinum, large cystic areas in the right costophrenic and cardiophrenic regions, a small rounded shadow in the right mid-lung field, similar small rounded shadows in the left mid-lung field, and a markedly enlarged and deformed left cardiac shadow. An electrocardiogram containing only the standard leads was within normal limits. The patient died four days after admission to the hospital. An autopsy revealed: (*1*) in the left ventricular myocardium, primary hydatid cysts which had ruptured into the ventricular lumen and disseminated into the greater circulation with hydatid implants in the brain, spleen, and kidneys, (*2*) rupture of the left ventricular cyst into the pericardium, producing pericardial hydatidosis, (*3*) a pericardial cyst opening into the right auricle and disseminating into the lesser circulation to produce an intra-arterial hydatid cyst within the lumen of the pulmonary artery and cuticular emboli in the lesser circulation. Primary pulmonary hydatidosis was also present. This is the third case of cardiopericardial hydatidosis described in the world literature as diagnosed during life, and the first with pulsus alternans.—*Equinococosis cardiaca, P. Parriel, V. Perez Fontana, O. Muras, & D. Mendoza, Torax, June, 1953,* ***2:*** *188.—(F. Perez Pina)*

Pulmonary Acariasis.—The chest roentgenogram of a young man who had had asthma

for seven months showed fine linear striations superimposed upon a "ground-glass" haze. A peripheral blood count revealed 36 per cent eosinophils. The sputum contained *Carpoglyphus* mites. The asthma did not improve with antispasmodic therapy, but responded to a course of acetarsol therapy.—*Pulmonary acariasis in Spain: An illustrative case report, M. deF. Taboada, Brit. M. J., February 20, 1954, No. 4859: 437.—(E. A. Riley)*

Blood and Sputum Eosinophils.—Among 205 African natives studied simultaneously for sputum eosinophilia and eosinophilia in the peripheral blood, nearly two-thirds had 500 or more eosinophile leukocytes per cubic millimeter of blood. Three-quarters of the patients showed an increasing frequency and density of the eosinophils in the sputum as the blood eosinophilia increased. In approximately one-quarter of the patients, however, there was no correlation between blood and sputum eosinophils.—*Eosinophils in the sputum, J. Vaughn, Brit. M. J., January 2, 1954, No. 4852: 27.—(E. A. Riley)*

Lung Cysts in Xanthomatosis.—Xanthomatosis is occasionally associated with cystic changes in the lung. Xanthomatosis may involve the skin, dura, orbit, pituitary gland, brain, liver, spleen, lymphatics, bone, tracheobronchial tree, lung, and pleura. Pulmonary cystic changes were observed in 4 patients with the normocholesteremic type of primary essential xanthomatosis. The symptoms in these cases consisted of cough, expectoration, blood-streaking, fatigability, chest pain, weight loss, and afternoon fever. Chest roentgenograms showed numerous bilateral nodular infiltrations, bilateral irregular stringy densities with cystic areas or extensive soft-appearing infiltrates containing areas of lucency. One of the patients had xanthomatous lesions of the peripheral lymph nodes, bronchus, skin, and muscle as well as lung. Another had numerous destructive bony lesions and involvement of the gum. The pulmonary alterations in xanthomatosis are considered as being due to two factors: (*1*) a granulomatous process involving the pulmonary interstitial tissues and (*2*) bronchiolar obstruction. It may be difficult to differentiate the proliferative and granulomatous phases of xanthomatosis from neoplasm as the characteristic xanthoma cells are seen only in the more mature lesions. Widespread tissue involvement, undifferentiated microscopic findings, and little deterioration of health suggest xanthomatosis. The cystic changes may be due to pulmonary interstitial involvement and bronchiolar obstruction. Hand-Schüller-Christian disease, Letterer-Siwe disease, lipoid granulomatosis, and eosinophilic granuloma of bones and lungs may be mere facets of primary normocholesteremic xanthomatosis.—*Pulmonary cystic changes in xanthomatosis, J. Forsee & H. Blake, Ann. Surg., January, 1954, 139: 76.—(M. J. Small)*

Diffuse Interstitial Pneumonitis.—A 57-year-old man was hospitalized with the chief complaints of dyspnea, ankle swelling, and blueness of his fingernails. His chest film showed vascular congestion, pulmonary emphysema, and fibrosis. The liver was markedly enlarged. Significant laboratory findings were a hemoglobin level of 17.5 gm. per 100 cc., 6,700,000 erythrocytes per cu. mm., and a hematocrit of 65 per cent. A lung biopsy revealed chronic interstitial fibrosing pneumonitis. The patient died after first responding to treatment for congestive failure and secondary polycythemia. At necropsy, the histologic findings in the lungs were most distinctive. Large quantities of partly hyalinized connective tissue were diffusely deposited, and many alveoli were obliterated. There were few inflammatory cells. The peribronchial and perivascular spaces also showed some fibrosis.—*Diffuse interstitial fibrosing pneumonitis, J. J. Kirshner, R. L. Breckenridge, F. A. Allbritten, Jr., & P. A. Theodos, J.A.M.A., January 23, 1954, 154: 336.—(H. Abeles)*

Interstitial Fibrosis of Lungs.—Three new cases of diffuse interstitial pulmonary fibrosis of lungs and 20 reported cases show

it to be a chronic progressive, diffuse, bilateral disease which occurs in adults. Clinically, it is characterized by dyspnea, cough with expectoration, and cyanosis. Cor pulmonale and polycythemia may develop. Pathologically, there is diffuse alveolar wall hypertrophy on the basis of capillary proliferation. This angiosis is accompanied by reticular hyperplasia. Collagen may increase in the hypertrophic walls. The etiology of the disease is unknown.—*Diffuse interstitial fibrosis of lungs: A form of interstitial angiosis and reticulosis of the lungs, A. Golden & T. T. Bronk, A. M. A. Arch. Int. Med., November, 1953, 92: 606.*—(*G. C. Leiner*)

Cough Syncope.—Sudden syncope may follow a vigorous cough in middle-aged men who are robust, extroverted, and indulge heavily in smoking, drinking, and eating. The cough is dry, unproductive, and often is a cascading paroxysm, accompanied by extremely vigorous muscular efforts. At times, only one sharp bark precedes syncope. Burning or tingling in the laryngeal region is described by some at the onset of the cough. Chronic pulmonary disease, such as emphysema or bronchial asthma, is often present. Bronchiectasis, pneumoconiosis, sarcoidosis, acute pneumonia, and acute bronchitis have also been associated with the syndrome. For each attack in which consciousness is lost, there may be many minor episodes of giddiness and diminished vision. Usually after a few coughs there is no desire to breathe, a little giddiness and dimness of vision appear, and suddenly consciousness is lost. Muscle relaxation is complete and the patient falls or slumps. The face is turgid and congested, later becoming pale. Diaphoresis often ensues. Convulsions, which occur in less than 10 per cent of the patients, are clonic and often limited. The attack is brief, often lasting only a few seconds. Frequently the patient arises, resumes his activity or conversation, and recalls only that he coughed. The attack is generally regarded as of little consequence, which accounts for the apparent low incidence of the syndrome. In many instances, the sensation is described as pleasant. Unlike certain other types of syncope, more than half of the attacks occur in the lying or sitting position; often they appear during or immediately after a heavy meal. A brief warning, sufficient to prevent serious injury, is experienced by some patients; a few can abort an attack by holding the breath or firmly grasping an object for support. The number of attacks varies from a single episode to thirty per day. The incidence parallels the course of the underlying respiratory disease; when this is self-limited or remediable, they disappear with its passing. With recurrent chronic diseases, many attacks occur over several decades and one patient had 500 to 1,000 attacks in a nine-year period. Although the attacks are generally stated to be benign, the authors have witnessed one death. The differential diagnosis is relatively easy because syncope is always preceded by a cough. The laryngeal crises of tabes dorsalis, a rare condition, may imitate the cough syndrome in every detail. Treatment consists in eradicating the underlying cause of cough and in diminishing the sensitivity of the cough reflex. Cocainization of particularly sensitive areas and procaine block of the superior laryngeal nerve have been useful. Smoking and excessive alcohol should be discouraged; the obese should be urged to reduce. Atropine in full doses has not been useful. No drug can simultaneously offset the adverse effects of pulmonary hypertension and peripheral hypotension. Patients cannot voluntarily reproduce the syncope, which has greatly hindered its investigation.—*The syndrome of cough syncope, A. Kerr, Jr. & V. J. Derves, Ann. Int. Med., December, 1953, 39: 1240.*—(*T. H. Noehren*)

Bronchodilators for Emphysema.—Positive-pressure oxygen inspiration, inhalation of an oxygen-generated aerosol of isopropyl arterenol (Isuprel®), or both were given for two to three weeks to 41 patients with chronic diffuse obstructive emphysema. The therapeutic results, judged chiefly by symptoms and pulmonary function tests, indicated that aerosolized Isuprel® was superior to oxygen breathing alone and as good as the combined

treatment. Most patients' symptoms improved moderately when they were given an oxygen-generated Isuprel® aerosol, either with or without positive-pressure breathing. Dyspnea persisted, although variably reduced, and the results of pulmonary function tests were unchanged, indicating that the basic broncho-pulmonary changes were not altered by any of the treatments.—*Treatment of pulmonary emphysema with aerosolized bronchodilator drugs and intermittent positive-pressure breathing, W. S. Fowler, H. F. Helmholz, Jr., & R. D. Miller, Proc. Staff Meet., Mayo Clin., December 30, 1953, 28: 743.—(E. A. Riley)*

Hypoxemia in Emphysema.—The arterial oxygen saturation of 240 patients with chronic diffuse obstructive emphysema was measured by oximetry while the patients were resting, exercising, and breathing 90 to 95 per cent oxygen. Half of this group maintained normal arterial oxygen saturation, even after exercising to their tolerance limit; 23 per cent had hypoxemia at rest; the remaining 27 per cent had normally saturated arterial blood at rest but became hypoxemic during a standard exercise test. Although hypoxemia was more common in more disabled patients, the presence or absence of hypoxemia did not govern the degree of disability. Many patients with hypoxemia tolerated exercise fairly well, and numerous patients with normal arterial oxygen saturation had severe exertional dyspnea. This was shown by the clinical history as well as by exercise tests. Cor pulmonale with congestive failure occurred almost exclusively among patients who had transient or persistent hypoxemia and chiefly among patients with persistent hypoxemia. Only one case of congestive failure and cor pulmonale occurred among the 118 patients with normal arterial oxygen saturation at rest and exercise; 18 instances of congestive right heart failure occurred among 122 patients with persistent or transient hypoxemia.—*The relationship of arterial hypoxemia to disability and to cor pulmonale with congestive failure in patients with chronic pulmonary emphysema, R. D. Miller, W. S. Fowler, & H. F. Helmholz, Jr., Proc. Staff Meet., Mayo Clin., December 30, 1953, 28: 737.—(E. A. Riley)*

Abnormal Pulmonary Air Spaces.—Clinical and pathologic observations have shown that air space abnormalities described as cysts, bullae, and pneumatoceles are common and are probably becoming more frequent. They are practically always acquired and are closely related to, or in fact are, emphysematous changes in the lung. The observations have emphasized how necessary it is to explain, using the concepts of emphysema, abnormal air spaces which frequently show morphologic features of developmental origin as well as the variable air space abnormalities. A new concept considers the changes, including emphysema, as forms of an air space disorder which is a disturbance of the lung's visceral function.—*Clinical observations and interpretations of abnormal air spaces in the lungs, a new concept of their origin, E. Mayer & I. Rappaport, J.A.M.A., October 24, 1953, 153: 700.—(H. Abeles)*

Respiratory Dead Space for Various Gases.—(*1*) Using a rapidly recording mass spectrometer and a light weight spirometer with attached potentiometer, the respiratory dead space was estimated with oxygen, carbon dioxide, nitrogen, and helium as indicator gases. (*2*) In 5 normal subjects ranging in age from 27 to 35 years, the dead space decreased to the same degree with increasing breath-holding times for all four indicator gases. (*3*) The dead space for the four indicator gases was essentially the same in 3 of 5 subjects, and in the other 2 the dead space for helium appeared to be somewhat (20 ml.) smaller than for the other indicator gases. Breathing helium did not decrease the oxygen carbon dioxide or nitrogen dead spaces. (*4*) Using the mass spectrometer simultaneously with a Lilly nitrogen meter, expiratory gas concentration curves were obtained in 5 subjects for oxygen, carbon dioxide, and nitrogen; these were so similar that there was no measurable difference in dead space volume (Authors'

summary).—*The respiratory dead space measured by single breath analysis of oxygen, carbon dioxide, nitrogen or helium, J. Bartels, J. W. Severinghaus, R. S. Forster, W. A. Briscoe, & D. V. Bates, J. Clin. Investigation, January, 1954, 33: 41.*—(*E. Dunner*)

Developmental Anatomy of Lungs.—Human embryos were studied by means of the dissecting microscope, microscopic sections, and wax reconstructions of the developing bronchial tree. These studies, with those of Lδosli and Potter, indicate that there are 3 stages of bronchopulmonary developmental differentiation: (*1*) a glandular period during which the bronchial divisions are established but during which respiration would be impossible; (*2*) a canalicular period, from the fourth to the sixth month of intrauterine growth, when terminal air spaces develop as long epithelium-lined channels; (*3*) the alveolar period during which the alveoli are formed, apparently as capillary loops invade the elongating air channels. The original cuboidal epithelial lining of the air channels seems to disappear because it is separated by intruding capillaries and scattered by elongating and distending peripheral air spaces. At birth, 18 generations or subdivisions of the bronchi can be counted, but this growth and subdivision continue postnatally. Branching increases during childhood so that the adult has 23 to 25. The developing segments and segmental bronchi often vary from the standard pattern in the embryo and in the adult. Thus, in 16 per cent of the specimens, the right upper lobe contained 4 rather than 3 segments and, in 27 per cent, the left upper lobe had 5 segments. The lungs of uniovular twin embryos may thus differ, suggesting a somatic rather than a genetic influence on the developing bronchial tree.—*Observations on the anatomy and development of the lungs, E. A. Boyden, Journal-Lancet, December, 1953, 73: 509.*—(*E. Rothstein*)

Anomalous Pulmonary Veins.—In anomalous pulmonary drainage, the blood from the lungs drains into the right atrium directly or into a tributory vein and so fails to enter the left atrium. In a physiologic sense, this occurs when the veins are normal but the atrial septum has a defect. The anomalous return may be total and partial. If total, no pulmonary veins connect with the left atrium and all the arteriolized blood enters the right atrium. Some of this oxygenated blood flows through an atrial septal defect and thus enters the systemic arterial circulation; left-to-right and right-to-left shunts always coexist in this syndrome, one of the cyanotic congenital cardiac diseases, and arterial oxygen saturation is incomplete. If partial, the anomalous pulmonary venous connections form one of the acyanotic congenital heart diseases; functionally, they resemble uncomplicated atrial septal defects with only a left-to-right shunt. Patients with completely anomalous pulmonary venous connections rarely survive infancy. The occasional patient who survives to adulthood generally has a small septal defect. In contrast, patients with a partial anomalous connection often live to adulthood; they have little disability if less than half of the blood is drained anomalously. If more than half of the blood is drained anomalously, the right ventricle may fail. Approximately 135 cases of anomalous drainage have been reported. Approximately half of these patients had totally anomalous connections, often accompanied by other major anomalies. Of 5 cases of anomalous pulmonary connection seen during the past five years, 3 were total and 2 were partial. Anomalous pulmonary venous connections usually occur when the developing atrial region fails to join the pulmonary portion of the splanchnic plexus or when the normal communications between the atrium and the splanchnic plexus are secondarily obliterated. Structures, such as bronchi and arteries, which develop simultaneously perhaps interfere with the early pulmonary veins. A cardiac catheter may pass from the right atrium through a patent foramen ovale or septal defect into the left atrium and thence into a pulmonary vein, thus diagnosing the anomaly. The right pulmonary veins are abnormal ap-

proximately twice as often as the left. In any one given case, all of the anomalous veins usually empty into one structure. The anomalous pulmonary veins terminate, in order of descending frequency, into the superior vena cava, the right atrium, the left innominate vein, the coronary sinus, and the azygos vein. Less commonly, they empty into the portal vein, the ductus venosus, the inferior vena cava, and the left subclavian vein.—*Pathologic and developmental considerations in anomalous pulmonary venous connection, J. R. Edwards, Proc. Staff Meet., Mayo Clin., August 26, 1953, 28: 441.*—*(E. A. Riley)*

Diagnosis of Anomalous Pulmonary Veins.—A partially anomalous connection of the pulmonary vein may be difficult to differentiate from an atrial septal defect; they are functionally similar and frequently associated. Both anomalies must be considered when cardiac catheterization reveals the blood in the right atrium to be highly saturated with oxygen. If blood in the superior vena cava is highly oxygenated, an anomalous pulmonary vein probably drains into that vessel or into the innominate vein. If the anomalous vein drains into the inferior vena cava, the results are comparable. The cuvette oximeter is valuable in making these determinations. Fluoroscopy demonstrates the anomalous venous connection when the catheter enters the long field without passing through the cardiac shadow and delivers arterialized blood. If the veins drain directly into the right atrium, the right atrium contains oxygenated blood just as it does when there is an atrial septal defect; even if the catheter passes into the pulmonary fields, it may be impossible to determine whether it has passed through a septal defect or directly into a pulmonary vein. Even successive samples of blood may not prove an anomalous pulmonary venous connection when the catheter enters a pulmonary vein from within the cardiac shadow. An increased oxygen saturation of atrial, ventricular, and pulmonary arterial blood does not differentiate a partial anomalous pulmonary venous connection from an atrial septal defect. In the former condition, the pulmonary flow rarely is more than twice the systemic flow; in cases of atrial septal defect, shunt values of 70 to 85 per cent help exclude an anomalous venous connection as the sole cause of the increased flow. Without a septal defect, the ratio of pulmonary flow to systemic flow is governed chiefly by the proportion of pulmonary tissue drained anomalously. Arterial dilution curves after the injection of Evans blue differentiate the lesions more precisely, since the dyed blood's route to the arterial system affects the initial dilution pattern. Dye is injected successively into the right and left pulmonary arteries; the dilution curves demonstrate whether blood flowing through each lung is recirculated through the pulmonary circulation. This technique does not always disclose the site of recirculation. Patients with large defects and greatly increased pulmonary blood flow often shunt blood from right to left through the defect. In such cases, anomalous venous connection frequently cannot be distinguished from a septal defect, especially since they may coexist.—*Differential diagnosis at cardiac catheterization of anomalous pulmonary venous drainage related to atrial septal defects or abnormal venous connections, H. J. C. Swan, H. B. Burchell, & E. H. Wood, Proc. Staff Meet., Mayo Clin., August 26, 1953, 28: 452.*—*(E. A. Riley)*

Traumatic Bronchial Rupture.—Traumatic rupture of a bronchus in a six-year-old boy was complicated by severe subcutaneous emphysema. The resulting complete stenosis of the right main stem bronchus was successfully treated by pneumonectomy two months after the acute episode.—*Traumatic rupture of bronchus in a six year old boy treated by pneumonectomy, H. D. Dalgleish, G. M. T. Hazen, & W. S. Kinnear, Canad. M. A. J., January 1954, 70: 45.*—*(E. A. Riley)*

Tracheal Resection and Anastomosis.—A segmental sleeve resection of the trachea with end-to-end anastomosis gave a successful early result for a primary cylindroma. This

demonstrates the logic and availability of this procedure (*Authors' summary*).—*Resection and anastomosis of the intrathoracic trachea for primary neoplasms, J. E. Macmanus & R. McCormick, Ann. Surg., March, 1954, 139: 350.*—(*M. J. Small*)

Spontaneous Pneumothorax.—About one in every 1,000 patients admitted to the Philadelphia Naval Hospital has a spontaneous pneumothorax. Because of its frequency in young adult males, physicians should be familiar with all phases of the disease. Among 60 patients, only one had tuberculosis; 35 per cent showed a negative reaction to the tuberculin skin test. Tuberculosis thus seems not to be an important cause. The most common cause is probably the rupture of subpleural blebs and bullae. The physical activity of the patient at the time of onset bears no relationship to the attack nor do the symptoms have any relationship to the amount of collapse. Most patients respond satisfactorily to conservative management. If there is no change in the amount of collapse within five to seven days, then intrapleural, water-sealed catheter drainage should be instituted. Certain clinical problems dictate its use from the onset, namely: (*1*) tension pneumothorax, (*2*) a physiologically impaired contralateral lung, and (*3*) associated cardiac disease with marked dyspnea. The most common complication is hydrothorax and usually this absorbs spontaneously.—*Spontaneous pneumothorax, M. R. Jones & H. A. Lyons, Am. J. M. Sc., January, 1954, 227: 13.*—(*W. J. Steininger*)

Postpartum Spontaneous Pneumoperitoneum.—Pneumoperitoneum appeared spontaneously in a 23-year-old woman sixteen days after a normal, full-term, spontaneous, uncomplicated delivery. Symptoms developed three hours after postpartum exercises consisting of sit-ups and the assumption of the knee-chest position. Exploratory laparotomy was negative. It was assumed that air entered the peritoneal cavity through the genital tract during knee-chest exercises.—*Spontaneous pneumoperitoneum, L. L. Bean & R. I. Garrett, U. S. Armed Forces M. J., February, 1954, 5: 375.*—(*E. A. Riley*)

Dyspnea in Heart Disease.—Several factors of variable importance are responsible for the occurrence of dyspnea in heart disease. Foremost among these is the mechanical impairment of the respiratory movements, which can be explained only in part on the basis of pulmonary rigidity caused by congestion. A bronchial asthmatic factor can be detected in nearly all cases of heart failure and is occasionally found to be the main cause of dyspnea. In comparison, hyperventilation due to change in blood composition or to decreased circulation in the respiratory center is considered of secondary importance in the pathogenesis of dyspnea (Authors' summary).—*Das Problem der kardialen Dyspnoe, F. Wyss & J. Regli, Schweiz. med. Wchnschr., December 5, 1953, No. 49: 1175.*—(*E. Dunner*)

Incidence of Cancer.—In a series of 3,946 consecutive necropsies of male veterans in Los Angeles from 1948 through 1952, there were 1,498 cases of one or more malignant neoplasms. Primary carcinoma of the lung was found in 329 of these cases (21.9 per cent of all malignant neoplasms and 8.33 per cent of all autopsies). This was the commonest malignant neoplasm. Epidermoid carcinoma was the most frequent type; undifferentiated carcinoma was second; and adenocarcinoma was third in frequency. The right lung was the primary site oftener than the left and the upper lobes oftener than the lower. The average age for patients with carcinoma of the lung was 57.63 years. The youngest patient was 25 and the oldest was 83 years of age. The following groups of malignant neoplasms ranked second to tenth in order of frequency: lymphomas and leukemias, carcinoma of the prostate, carcinoma of the large intestine, mostly sigmoid and rectum, carcinoma of the stomach, primary intracranial tumors, carcinoma of the pancreas, carcinoma of the bladder, carcinoma of the kidney, and carcinoma of the larynx.—*Primary carcinoma of the lung in the male*

veteran, K. M. Earle, A. M. A. Arch. Path., February, 1954, 57: 106.—(E. Bogen)

Intrathoracic Vagus Tumor.—Intrathoracic tumors rarely arise from the vagus nerve, but many intrathoracic neurofibromas become malignant. A 63-year-old man became hoarse and later had left chest pain. The fluoroscopy revealed a shadow in the left side of the chest anterior to the aorta. A tumor, the size of an apple, was removed from its site adjacent to the aortic arch, where its lower end blended with the vagus nerve. Histologic examination revealed an edematous, partially necrotic neurofibroma. A few months after the operation, the mediastinal lymph nodes enlarged, and the patient died six months after the operation.—*Intrathorakaler neurogener Vagustumor, G. Wense, Wien. klin. Wchnschr., January 22, 1954, 66: 48.—(G. C. Leiner)*

Thoracic Fibrosarcoma.—Among 86 malignant intrathoracic tumors, 4 (4.6 per cent) were fibrosarcomas. The degree of malignancy was not only variable but often disputable. The same tumor might be called "fibrosarcoma" by one competent pathologist and "fibroblastic tumor offering risk of local recurrence" by another. The site of origin has often been impossible to determine, especially in large tumors. They have arisen from visceral pleura, diaphragm, lung, mediastinum, or chest wall. Trauma appeared to play a part in 2 of the 4 cases. Two patients had pleural effusion without evidence of pleural metastases. Pulmonary osteoarthropathy was severe in one patient; it disappeared rapidly and completely after resection. All of the patients complained of pain, chiefly of an intercostal neuralgia type; the 2 who had voluminous tumors were dyspneic. The diagnosis was suggested by roentgenogram but could not be precise until the tumor was examined histologically. The tumors weighed 100 to 3,500 gm. In each instance, the tumor could be separated from the adjacent lung. The surrounding tissue was never invaded and, in the brief postoperative follow-up, there has been no metastasis or local recurrence. Sacrifice of normal lung in removing such tumors is never justified.—*Le fibrosarcome thoracique, A.-P. Naeff, Poumon, February, 1954, 10: 133.—(F. S. Lansdown)*

Pulmonary Chondro-Hamartomas.—Chondro-hamartomas of the lung are rare but 2 cases were recently encountered. The first was in a 35-year-old man who had had a few weeks of mild hemoptysis. Roentgenographic examination showed a spherical retrocardiac opacity bordering the left ventricle. At operation, the hard, well-delimited, white tumor was 4 cm. in diameter. Histologically, it was bounded by unstratified cuboidal epithelium, was relatively avascular, and contained fibromatous, chondromatous, and myxomatous tissue penetrated by digitations of the peripheral epithelium. These tissues had remained embryonal. The second tumor was in a 45-year-old woman who was followed fourteen years after a thoracic tumor was discovered on routine roentgenographic examination. Because she developed right paravertebral pain radiating anteriorly and a sensation of restricted respiration, she consented to an operation. The only abnormal physical finding was a slight collateral circulation over the left hemithorax. Roentgenographically, a round mid-paramediastinal shadow the size of an orange lay in the right costovertebral gutter. At operation the large tumor occupied the posterior portion of the main fissure, intimately adhering to the visceral pleura of the upper and middle lobes. The partly atelectatic lower lobe was separated easily and the tumor was freed to the bottom of the interlobar fissure. There it was directly implanted on the main bronchus at the exit of the right middle lobe bronchus. This implantation was a short bronchial communication with a thin fibrous wall and was 4 or 5 mm. in diameter. Below this patent bronchial connection was a branch of the pulmonary artery. The 7 cm. tumor was cauliflower-shaped and weighed 220 gm. Section was difficult because the tissue was bony. Histologically, the tumor contained cartilagenous areas in the process of ossification, cartilage-

nous areas like chondromas, myxomatous areas with stellate cells, fibrous areas and fibrocytes, areas of acinar glands, and, deep in the fibrous and myxomatous areas, plasmacytic nodules. These tumors are uniformly benign, easily removed, and need be resected only because the preoperative diagnosis is uncertain.—*Les chondro-hamartomes pulmonaires, E. Nègre, G. Martin, & R. Loubatières, Poumon, January, 1954,* ***10:*** *5.—(F. S. Lansdown)*

Betatron Radiation for Thoracic Neoplasm.—Palliation in thoracic neoplasms is judged by the objective local effects, alteration in clinical symptoms, and the patient's general condition, useful life, absolute survival time, and the duration of the terminal distress. The 23 mev betatron roentgen beam produced unusually good palliation and possibly cured patients with the Pancoast type of tumor. It provided better than average palliation with commoner advanced bronchogenic cancers and good palliation with possible cures in early primary esophageal neoplasms. Palliative and curative therapy were planned alike. The superior results with the betatron as compared with conventional roentgen rays was due to more adequate and uniform depth dose distribution with the former.—*Radiation management of otherwise hopeless thoracic neoplasm, L. L. Haas, R. A. Harvey, & S. S. Langer, J.A.M.A., January 23, 1954,* ***154:*** *323.—(H. Abeles)*

ANTIMICROBIAL THERAPY

Large Doses of Isoniazid in Children.—From February, 1952, to June, 1953, 84 children, several months to fourteen years of age, were treated with isoniazid. Tuberculous meningitis was present in 22 cases, tuberculous pleurisy, peritonitis, or pericarditis in 8 cases, renal tuberculosis in one case, nodular and cavitary-nodular pulmonary tuberculosis in 6 cases, and simple primary tuberculosis in 47 cases. Large daily doses of isoniazid were always used; less than 10 mg. per kg. in 4 cases, 10 to 20 mg. per kg. in 29 children, 20 to 30 mg. per kg. in 40 patients, and 30 to 40 mg. per kg. in 11 cases. While 5 patients were treated for less than one month, 18 received the large doses for two to three months, 19 for three to four months, 11 for four to five months, 3 for five to six months, and 5 for six to seven months. Of the 84 children, 75 showed no drug intolerance. Hematologic studies of 15 children given more than 20 mg. per kg. daily showed no alteration of the erythrocytes, a 10 per cent leukopenia, a 20 per cent neutropenia, and an increase of 2 or 3 per cent in the eosinophils. All liver function tests remained normal except that galactose excretion was slightly delayed in 6 of 15 children. Kidney function tests were normal. The isoniazid blood concentrations were high, being 2 to 3 γ per ml. with doses of 10 mg. per kg, 6 to 10 γ with doses of 20 to 30 mg. per kg., and 10 to 25 γ with doses of 40 mg. per kg. Such concentrations are not always needed, but they can be useful in serious cases or when tubercle bacilli are initially resistant to isoniazid. A four-year-old child with tuberculous meningitis had tubercle bacilli resistant to 10 γ of isoniazid per mg. Doses of 30 to 40 mg. per kg. produced complete recovery.—*Posologie de l'hydrazide de l'acide isonicotinique (INH) chéz l'enfant, R.-A. Marquézy, Ch. Bach, & J. P. Clermont, Presse méd., November 28, 1953,* ***61:*** *1569.—(V. Leites)*

Large Doses of Isoniazid.—Three daily doses of isoniazid, 250 mg., produced blood concentrations of 3 to 7.5 per ml. This dosage was remarkably well tolerated; of 70 patients, only one developed polyneuritis, which subsided quickly when treatment was stopped. The effects exceeded those obtained with the usual dosage. The high doses are now used in a "mass attack" on pulmonary tuberculosis, being given with intermittent streptomycin, intravenous *p*-aminosalicylic acid, and a

sulfone. This regimen is continued for a maximum of six weeks and is then replaced with a maintenance dose of isoniazid, 250 mg. twice daily.—*Taux de concentration dans le sang del'isoniazide administrée "per os" sous forme d'une triple dose quotidienne de 250 mg., R. Benda, R. Movelec, & Mme. Guilbert, Rev. de la tuberc., 1953, 17: 1067.—(V. Leites)*

Isoniazid with Other Drugs.—The association of isoniazid with various antituberculous agents was studied in experimental tuberculosis of guinea pigs and rabbits. In guinea pigs, isoniazid and streptomycin showed no synergistic effect in doses less than half of the minimal active dose. Only doses of 0.5 mg. of isoniazid and 2 mg. of streptomycin were capable of preventing, even inconstantly and incompletely, the development of abscesses and ulcerations. The results were no better than those obtained with isoniazid alone. Isoniazid and *p*-aminosalicylic acid (PAS) had considerable synergistic effect; 0.4 mg. of isoniazid and 75 mg. of PAS were sufficient to inhibit totally the formation of abscesses and ulcerations in the infected animals. Combinations of isoniazid and sulfones also showed synergism; 0.4 mg. of isoniazid and 75 mg. of sulfone produced rapid healing of minimal lesions a few days after inoculation. In experimental tuberculosis of rabbits there was no synergistic effect of isoniazid and streptomycin in doses smaller than the minimal active dose of each drug. Isoniazid in doses equal to, or greater than, the minimal effective dose given with equivalent doses of streptomycin inhibited for long periods the appearance of roentgenographic lesions, even if treatment is carried out for only thirty days. This effect is definitely superior to that obtained with isoniazid alone, even in high doses. Isoniazid and neomycin, even in high dosage, did not produce the same effects.—*Étude expérimentale in vivo de l'association de l'I.N.H. a diverses substances antibacillaires (streptomycine, P.A.S., sulfone, néomycine, actiline), Ch. Gernez-Rieux, A. Taquet, M. Fabre, & C. Voisin, Rev. de la tuberc., 1953, 17: 916.—(V. Leites)*

Susceptibility to Isoniazid.—From 50 patients, 380 sputum samples were obtained at fifteen-day intervals before and during treatment with isoniazid. The samples were tested for isoniazid susceptibility by both direct and indirect methods. By the direct method, at the end of eleven months of treatment, the results were as follows: (*1*) In 10 patients (20 per cent), the presence or absence of resistance could not be determined, (*2*) in 15, (37.5 per cent of the cases in which resistance could be determined), the cultures were resistant. With the indirect test, the results were variable and almost always inconsistent.—*Determinación de la sensibilidad de mycobacterium tuberculosis a la isoniazida, L. F. Bojalil, A. Monnier, & P. Ramírez, Rev. mex. de tuberc., May-June, 1953, 14: 291.—(F. Perez Pina)*

Chemotherapy of Pulmonary Tuberculosis.—Two groups, each containing 100 patients with active pulmonary tuberculosis, were treated for six months with two different regimens of chemotherapy. The first group received 1 gm. of streptomycin twice weekly and 14 gm. of sodium para-aminosalicylic acid daily. The second group was given these two drugs in identical doses and also received 225 mg. of isoniazid daily. The second group included more minimal cases and correspondingly fewer moderately advanced cases; the two groups did not differ significantly as to type or pattern of disease. Cavitation was present at the onset of therapy in 66 per cent of the "2 drug" group and in 53 per cent of the "3 drug" group. Pneumoperitoneum was used for 26 patients in the first group and for 12 patients in the second. Clinical symptoms and the weight gain were the same in the two groups after six months. Definite roentgenographic clearing occurred in 76 per cent of the "2 drug" group and in 81 per cent of the "3 drug" group. At the end of six months, planographic studies showed cavity closure in 53 per cent of the "2 drug" group and in 64 per cent of the "3 drug" group. Of the "2 drug" group, 84 per cent had sputum conversion by culture, compared with 98 per cent

of the "3 drug" group.—*Streptomycin and PAS vs. streptomycin, PAS, and isoniazid in the treatment of pulmonary tuberculosis, A. W. Capon, Canad. M. A. J., January, 1954, 70: 62.—(E. A. Riley)*

Neomycin Ototoxicity.—The ototoxic effects of neomycin in human patients can be substantiated anatomically and histologically in guinea pigs. Massive doses of neomycin given to 2 guinea pigs caused deafness rapidly. The inner and outer hair cells disappeared from the organ of Corti, followed by an ascending degeneration of the auditory nerve. In contrast to streptomycin, neomycin damages the cochlea. Neither functional nor histologic changes were noted in the vestibular apparatus.—*Vorläufige Mitteilung über die toxische Wirkung von Neomycin auf das Gehörorgan des Meerschweinschens, L. Ruedi, D. Graf, & B. Tschirren, Schweiz. med. Wchnschr., October 3, 1953, 83: 1117.—(E. Dunner)*

Hypersensitivity to PAS.—Thrombocytopenia and hematemesis occurred in a patient who had received sodium *p*-aminosalicylic acid (PAS). Giving PAS again caused thrombocytopenia during two test periods. The reaction was apparently a hypersensitivity with platelet agglutination and destruction as well as megakaryocyte maturation arrest.—*Thrombocytopenia induced by sodium para-aminosalicylic acid: Report of a case, H. A. Wurzel & R. L. Mayock, J.A.M.A., November 21, 1954, 156: 1094.—(H. Abeles)*

Nitrogen Mustard for Tuberculous Lymphadenitis.—Nine patients, mostly youngsters, with superficial tuberculous lymphadenitis were given nitrogen mustard intravenously. Instead of the standard daily 0.1 mg. per kg., an initial dosage of 1.2 to 2.5 mg. was employed. This gradually increased but never exceeded 5 mg. The total dose, frequency, and interval between injections depended upon the severity of the disease, medication tolerance, the leukocyte count, temperature curve, and the clinical course. As a result, one patient received a total of 13 mg. in five injections during a ten-day period. In other cases, 48 mg. were given in twelve injections during a two-month period, with intervals of one to eight days. Therapeutic results were achieved relatively rapidly. There were no relapses in 3 cases observed for one year or in other cases observed two to eight months. Nitrogen mustard injections are the least expensive and quickest way to treat tuberculous lymphadenitis.—*Die Stickstoffsenfgastherapie der tuberkulosen Lymphome, G. Bovo & B. D'Agnolo, Schweiz. med. Wchnschr., November 14, 1953, 83: 1117.—(E. Dunner)*

Corticotropin for Tuberculous Meningitis.—In an attempt to avoid thick basal exudates and tuberculous endarteritis, 31 Negro children with tuberculous meningitis were treated with corticotropin and isoniazid. Of the 31 patients, 18 also received streptomycin and *p*-aminosalicylic acid. It was hoped that corticotropin would control the cellular reaction, leaving the tubercle bacilli free for antibiotic attack rather than enmeshed and inaccessible. In 1950, the over-all mortality rate from tuberculous meningitis was 60 per cent. Earlier diagnosis and the prolonged use of daily intrathecal streptomycin reduced the mortality to 10 per cent in 1951. The mortality for the present patients treated with corticotropin was 6.45 per cent. Patients with tuberculous meningitis treated with corticotropin and dying from other causes have not had the characteristic basal exudate. The dosage of corticotropin was 6 to 25 international units intramuscularly every six hours or 12 to 50 international units of the gel twice daily subcutaneously for a week or longer. The administration of corticotropin provoked no evident spread of pulmonary tuberculosis. Intrathecal streptomycin is no longer needed in the treatment of tuberculous meningitis.—*Tuberculous meningitis treated with ACTH and isoniazid, W. C. M. Bulkeley, Brit, M. J., November 21, 1953, No. 4846: 1127.—(E. A. Riley)*

New Isoniazid Derivative.—G 605 is a compound molecule of isoniazid and benzalde-

hyde metalsulfuric acid with a high chemotherapeutic index. The free acid G 605 by weight is 45 per cent isoniazid, the sodium salt is 34.4 per cent isoniazid. The 38 patients treated with this drug averaged twenty-seven years of age and had extensive, fresh, cavitary-nodular or pneumonic tuberculosis. Some had never received chemotherapy; others had received small doses of streptomycin and *p*-aminosalicylic acid (PAS). Still others had not responded to streptomycin, PAS, and isoniazid. The patients were divided into three groups and treated daily with G 605: (*1*) intravenously with 4 gm., (*2*) orally with 3 to 4 gm., or (*3*) with both oral and intravenous administration of 2 to 3 gm. and 4 gm., respectively. Treatment lasted an average of 78 days. The drug was well tolerated; 3 patients had side reactions of shock due to too rapid infusion, urticaria, transient unconsciousness during an infusion followed by paresthesias in the legs for a few days. The renal or hepatic function never became abnormal. The effects on the general condition were excellent; 40 per cent gained 1 to 5 kg.; 17 per cent, 5 to 10 kg.; and 9 per cent, more than 10 kg. The sedimentation rate became normal in 60 per cent within ten to thirty days. Sputum conversion occurred in 48 per cent. Roentgenographically, the lesion changed little or not at all in 31.3 per cent; definite improvement was seen in 68.7 per cent with marked improvement in 13 cases and very marked improvement in 6. Considerable clearing was, for instance, observed within two months in a case of tuberculous pneumonia of the left upper lobe which had not responded to concomitant streptomycin, PAS, and isoniazid. G 605 diminished or closed fresh cavities within one or two months, but older lesions responded poorly.—*Étude et clinique d'un derivé de l'isoniazide: le G 605, A. Duroux, P. Masson, J. Marty, A. Jarniou, D. Azorin, Mistrot, & Robert, avec la collaboration de Girard & Destouches, Rev. de la tuberc., 1953, 17: 1092.*—(*V. Leites*)

Cyanacid.—Recently, Spanish investigators have produced a new antituberculous agent called cyanacid (Reazide®). Cyanacid has a distinct tuberculostatic effect *in vitro* against different strains, including isoniazid- and streptomycin-resistant tubercle bacilli. There exist, however, a primary and an induced resistance to the drug. Guinea pigs tolerated 50 mg. of cyanacid per kg. daily for sixty days. When given the drug prophylactically, all 3 animals remained free from lesions. When given after the experimental infection, cyanacid prevented lymphatic and hematogenous spread in all 5 treated animals.—*Erste Erfahrungen mit Reazide bei erperimenteller Tuberkulose, W. Hartl, Schweiz. Ztschr. Tuberk., January, 1954, 11: 65.*—(*E. Dunner*)

Cyanacid.—After cyanacid gave favorable therapeutic effects in experimental guinea pig tuberculosis, the drug was administered to 16 patients, 11 of whom have completed the prescribed course of therapy. Daily doses of 5 to 10 mg. per kg. produced a response in patients with pulmonary tuberculosis comparable to that with isoniazid. The drug was well tolerated orally except for minor side effects consisting of increased nervousness and parasthesias. The optimal dosage and combination therapy remain to be investigated. The preliminary results indicate that cyanacid can be used successfully when patients' tubercle bacilli are resistant to the classical tuberculostatic agents.—*Vorläufige Mitteilung über Beobachtungen bei Behandlung der Lungentuberkulose mit dem Hydrazid der Cyannessigsäure (Reazide®), H. Scheu, Schweiz. Ztschr. Tuberk., January, 1954, 11: 77.*—(*E. Dunner*)

Subtherapeutic Combination Therapy.—Since current opinions differ regarding the synergistic or antagonistic effects when streptomycin and isoniazid are combined, 80 guinea pigs were inoculated with tubercle bacilli and given subtherapeutic doses of streptomycin while they received small therapeutic doses of isoniazid. The guinea pigs were divided into four groups as follows: (*1*) control group, untreated; (*2*) treated with strepto-

mycin, 2 mg. per kg. per day; (*3*) given isoniazid, 3 mg. per kg. per day; and (*4*) given streptomycin and isoniazid. All medications were administered parenterally. An average tuberculosis index was calculated for each group, using a scale from zero to 20. Neither synergism nor antagonism were demonstrated in *Group 4*. The dose of streptomycin was truly subeffective, but that of isoniazid was too high and masked any synergistic action. A subsequent similar experiment using smaller doses of isoniazid, namely, 0.4 mg. per kg. of body weight, with the same dose of streptomycin demonstrated a definite synergistic effect. In the treatment of tuberculosis, combination therapy still offers the best approach.—*The effect of a subtherapeutic dose of streptomycin combined with a low dose of isoniazid in experimental tuberculosis in guinea pigs, S. Moeschlin & H. Austrian, Schweiz. Ztschr. Tuberk., January, 1954, 11: 56.—(E. Dunner)*

PABA Antagonism of PAS.—Rations containing varied amounts of para-aminosalicylic acid (PAS) with or without para-aminobenzoid acid (PABA) were fed to CF_1 mice prior to injecting *M. tuberculosis* H37Rv intravenously. The weights and survival times demonstrated that the chemotherapeutic activity of PAS against experimental tuberculosis is antagonized by PABA. Under natural conditions, however, the dietary intake of PABA in man or animals probably never approximates the amounts employed in this study.—*Antagonism of chemotherapeutic activity of p-aminosalicylic acid in experimental tuberculosis by p-aminobenzoic acid, R. H. Hubble & L. W. Hedgecock, Proc. Soc. Exper. Biol. & Med., December, 1953, 84: 526.—(E. Soto-Figueroa)*

LABORATORY STUDIES

Thymus Peptide and Tubercle Bacilli.—The local biochemical conditions partly determine the fate of tubercle bacilli within the body. Many physiologic tissue constituents inhibit or kill tubercle bacilli *in vitro*. The present observations show peptides to be antimycobacterial, as are the basic proteins like histones, protamines, and lysozyme. A stable, water-soluble substance was extracted with aqueous ethanol from calf thymus and tentatively named thymus peptide. Concentrations of 1 to 10 γ per ml. in an albumin liquid medium inhibited strains of mammalian mycobacteria, but had little or no effect on other microbial species. Among the mycobacteria, the attenuated bovine tubercle bacilli, BCG-Phipps, were the most sensitive; 1 γ of thymus peptide per ml. of medium retarded them. Virulent human strains were approximately ten times more resistant. High concentrations were required, however, to inhibit the growth of the avirulent H37ra strain, an avian strain, and *M. smegma*. The peptide was less inhibitory when the inoculum was large or when the medium was acidic. An enzymatic hydrolysate of casein or beef heart infusion broth antagonized the inhibition. Thymus peptide did not affect tubercle bacilli rapidly, but organisms exposed for longer than two weeks could not multiply in ordinary culture medium. Adding Tween® 80, a dispersing agent, did not alter the antimycobacterial activity of thymus peptide. Substances similar or identical to the thymus peptide were extracted from calf spleen, sheep thymus, beef lymph nodes, and calf pancreas but not from calf lung or calf liver.—*The antimycobacterial activity of a peptide preparation derived from calf thymus, R. J. Dubos & J. G. Hirsch, J. Exper. Med., January 1, 1954, 99: 55.—(J. S. Woolley)*

Thymus Peptide.—An extract of calf thymus possessed antimycobacterial activity *in vitro*. Chemically, the active substance was a basic peptide or a mixture of basic peptides, essentially free from other compounds but not yet homogeneous. The thymus peptide preparation was soluble in water and the lower alcohols. Its solubility was minimal between pH 10 and 11, suggesting an isoelectric point in

this range. The microbiologic activity of thymus peptide was destroyed by acid or alkaline hydrolysis and by trypsin digestion, but was unaffected by pepsin digestion. Cellulose membranes were permeable to thymus peptide. The basic amino acids, lysine and arginine, together accounted for approximately 40 per cent of the weight; no cystine and only traces of other amino acids containing sulfur were found. Thymus peptide may not occur as such in animal tissues. Since it was extracted at an acid pH, the peptide may have been produced by partial hydrolysis of histones, basic proteins which abound in the thymus. Similar or identical compounds extracted from organs other than the calf thymus have not been studied chemically.—*Chemical studies on a basic peptide preparation derived from calf thymus, J. G. Hirsch & R. J. Dubos, J. Exper. Med., January 1, 1954,* **99:** *65.—(J. S. Woolley)*

Antimycobacterial Activity of Peptides.—The antimycobacterial activity of calf thymus peptide under certain conditions *in vitro* was partially neutralized by increasing the concentration of sulfate ions in the medium and, to a lesser extent, by adding certain organic compounds which contain sulfur. Thymus peptide may inhibit tubercle bacilli by interfering with their sulfur metabolism. The peptide may bind or otherwise sequester sulfate ions, which are essential for the microorganisms' growth. Polylysine peptide and pituitary adrenocorticotropic hormone also are basic peptides derived from animal tissues and inhibit tubercle bacilli *in vitro*; their antimycobacterial activity is likewise antagonized by sulfate ions. Basic peptide hormones prepared from the posterior pituitary gland do not affect the growth of acid-fast bacteria.—*Mechanisms involved in the antimycobacterial activity of certain basic peptides, J. G. Hirsch, J. Exper. Med., January 1, 1954,* **99:** *79.—(J. S. Woolley)*

Toxicity of Silica.—Protein is adsorbed from solution as a film on quartz particles 1 to 3 γ in diameter. The amount adsorbed is a function of the protein solution's pH and concentration. The lack of specificity of the protein film on the quartz surface is nonspecific since the adsorbed film combines with specific antibodies and produces heterogeneous antibodies when injected into rabbits. When rabbit serum is adsorbed by quartz, the serum proteins in the film are so altered in some unknown manner that an agglutination reaction is clearly demonstrable. No material other than quartz produces agglutination titers in rabbits, even when injected as particles of comparable size. The protein structure of the adsorbed film is clearly altered, and quartz particles may be toxic because this provokes a foreign protein reaction in the tissues.—*Toxicity of silica, L. D. Scheel, B. Smith, J. Van Riper, & E. Fleisher, A.M.A., Arch. Indust. Hyg. & Occup. Med., January, 1954,* **9:** *29.—(T. H. Nochren)*

Chemosensitivity of Respiratory Center.—Perfusion of the cerebral ventricles of dogs anesthetized with morphine-chloralose, using solutions having an increased carbon dioxide and hydrogen-ion concentration, stimulated the respiration. Solutions with a decreased carbon dioxide and hydrogen-ion concentration depressed the respiratory activity. The results were the same whether the chemoreceptors were intact or denervated, and the solutions directly influenced the respiratory centers. During respiratory stimulation by an excess of carbon dioxide, the blood pH increased; the blood acidity increased when respiration was depressed by a carbon dioxide-poor solution. These changes in the blood pH were the result of altered respiratory activity. Because hydrogen-ion and carbon dioxide concentrations were changing simultaneously, the effects of these two factors could not be differentiated.—*Chemosensitivity of the respiratory center: Influence of CO_2 in the cerebral ventricles on respiration, I. R. Leusen, Am. J. Physiol., January, 1954,* **176:** *39.—(G. C. Leiner)*

Chemosensitivity of Respiratory Center.—The cerebral ventricles of dogs, anesthetized

with morphine-chloralose, were perfused after denervation of the chemoreceptors. Intraventricular changes in the carbon dioxide and hydrogen-ion concentration influenced the respiratory activity; an increased carbon dioxide and hydrogen-ion concentration stimulated respiration, while decreased concentration inhibited a respiration. Intraventricular alterations in the hydrogen-ion concentration, independent of carbon dioxide or bicarbonate ion, did not influence the respiratory activity. Alternating between perfusion solutions with identical pH but with different buffer concentrations produced a diphasic reaction. A solution with higher buffer concentrations initially slightly stimulated the respiration, which stabilized thereafter on a lower intensity. Perfusion with a solution containing a smaller buffer concentration reversed the response. The carbon dioxide/bicarbonate ratio in the cerebral ventricles thus influences the respiratory centers.—*Chemosensitivity of the respiratory center: Influence of changes in the H+ and total buffer concentrations in the cerebral ventricles on respiration, I. R. Leusen, Am. J. Physiol., January, 1954, 176: 45.—(G. C. Leiner)*

Pentobarbital and Respiratory Center.—Respiratory rhythmicity is highly susceptible to pentobarbital's depressant action. Initially, the drug slowed spontaneous breathing and decreased the threshold for a stimulus which evokes sustained apneusis. Subsequently, spontaneous respiration failed long before the respiratory center became inexcitable. As an early demonstrable effect on the respiratory center, amplitude of minimal responses changed appreciably. With progressive pentobarbital depression, all apneustic responses approached the level of spontaneous breathing. Early pentobarbital cumulation more markedly depressed thoracic apneustic responses, as evoked by stimuli of constant strength, than it did concomitant abdominal responses. Spontaneous breathing was similarly depressed during this period. Varying the stimulus voltage produced direct and generally equivalent effects in thoracic and abdominal responses. During light anesthesia, varying the stimulus frequency affected similarly the responses of the two respiratory components, but thoracic activity was more labile than its abdominal counterpart. After respiratory arrest, during deep anesthesia, reducing the stimulus frequency from 33 to 20 impulses per second almost abolished the thoracic apneustic response, whereas the abdominal response was reinforced. In 5 experiments, late pentobarbital cumulation made it necessary to use high voltage stimulating currents and the thoracic apneustic response became an active expiratory excursion which occurred simultaneously with diaphragmatic contraction.—*Effect of pentobarbital on electrical excitability of respiratory center in the cat, T. D. Harris & H. L. Borison, Am. J. Physiol., January, 1954, 176: 77.—(G. C. Leiner)*

Experimental Pulmonic Stenosis.—Infundibular pulmonic stenosis is the most common pulmonic stenosis in congenital heart disease. Such a stenosis might benefit one group of cardiac patients. These patients all have pulmonary hypertension and include those with the Eisenmenger complex, a single ventricle without pulmonary stenosis, a large ventricular septal defect, and true truncus arteriosus. At present, these abnormalities cannot be relieved surgically and their correction remains a problem. Now, infundibular stenosis has been produced experimentally. Right ventricular hypertension has persisted for a prolonged period, and certain congenital cardiac deformities with pulmonary hypertension might benefit from such a procedure.—*The experimental production of infundibular pulmonic stenosis, D. C. Sabiston, Jr. & G. R. Williams, Ann. Surg., March, 1954, 139: 325.—(M. J. Small)*

Myocardial Metabolism in Hypothermia.—Coronary blood flow and myocardial metabolism have been observed in the dog after immersion hypothermia. Although the coronary arteriovenous oxygen difference remained unchanged from the normothermic state, coronary blood flow and myocardial oxygen con-

sumption decreased. Aerobic energy uptake and left ventricular work both declined, but the proportionally greater fall in ventricular work suggested that the mechanical efficiency of the heart failed in the cold state. Glucose utilization by the myocardium generally decreased, but lactate and pyruvate usage were not consistently altered (Authors' summary). —*Coronary blood flow and myocardial metabolism in hypothermia, W. S. Edwards, S. Tuluy, W. E. Reber, A. Siegel, & R. J. Bing, Ann. Surg., March, 1954, 139: 275.—(M. J. Small)*

Cardiovascular Effects of Pulmonary Emboli.—Acute pulmonary hypertension was produced in 10 intact anesthetized dogs by injecting a 1 per cent suspension of lycopodium spores into the pulmonary artery. The rate of coronary outflow did not change significantly after this injection, although the mean pulmonary artery pressure was tripled. The cardiac output always increased after pulmonary hypertension was established, but the pulmonary artery pressure increased relatively more, so that the total pulmonary resistance increased significantly. The left ventricular oxygen consumption did not change; consequently, the left ventricular efficiency improved. At post-mortem examination, 5 of the dogs had lycopodium spores in the small vessels of all the pulmonary lobes but not in any other organ. Only one dog, which had received the largest dose of lycopodium spores, showed evidence at necropsy of having died of right-sided cardiac failure (Authors' summary).—*Cardiovascular effects of pulmonary embolization in intact dogs studied by venous catheterization of the coronary sinus, D. B. Hackel, T. D. Kinney, & W. T. Goodale, Am. J. Physiol., January, 1954, 176: 135.—(G. C. Leiner)*

PUBLIC HEALTH AND EPIDEMIOLOGY

Age and Reinfection.—The age incidence of serious secondary pulmonary tuberculosis interests all tuberculosis physicians. The primary infection can usually be dated by the appearance of a positive Mantoux reaction. To determine the age at which secondary infection may invade the lungs, it may be possible to measure the long latent period between a primary infection in later life and the eventual secondary pulmonary invasion. The 1930–1931 mortality rate of pulmonary tuberculosis among the French people from birth to seventy years old was compared with that for 1950–1951. In 1930–1931, pulmonary tuberculosis killed 32,000 males (160 per 100,000) and 23,500 females (110 per 100,000). In 1950–1951, it killed only 13,500 males (85 per 100,000) and 7,000 females (32 per 100,000). More patients in the former period died between the ages of thirty and forty-nine, regardless of sex; twenty years later, more men died between fifty and sixty-nine years and more women between the ages of thirty and forty. France's total population remained approximately 20,000,000. The number of cases of primary infections and new pulmonary tuberculosis registered during 1926 and 1951 indicate the pulmonary tuberculosis mortality is much lower under the age of thirty, and especially under 15, than in later life. In contrast to other forms of tuberculosis, typical phthisis does not often kill children younger than ten or even fifteen years. It is somewhat more fatal to girls than to boys. Such factors as the amount of a woman's manual labor seem to influence its frequency in later life. Infectious pulmonary tuberculosis occurs especially during puberty and early adult life. Among adults, phthisis follows primary infection after a latent period of approximately fifteen years.—*Rapport sur l'âge phtisiogène, E. Bernard & A. Lotte, Acta tuberc. belg., February, 1954, 45: 3.—(A. T. Laird)*

Arthritis and Lung Disease in Coal Miners. A new syndrome has been discovered among coal miners in the Rhondda Fach; rheumatoid arthritis is associated with nodular pulmonary fibrosis radiologically resembling but distinguishable from the fibrosis of pneumoconiosis.

Numerous discrete rounded opacities develop much more rapidly and diffusely throughout both lung fields. The lesions tend to appear in "crops". The lesions in each crop are similar in size and development, generally attain a diameter of 1 to 2 cm. within a few months, and then change little during many years. Cavitation, stellate scar formation, or calcification may eventually develop. The lesions occur only in men exposed to dust and do not resemble the interstitial pneumonitis previously associated with rheumatoid arthritis. So characteristic are these changes that rheumatoid arthritis could have been diagnosed from the chest roentgenograms with more than 50 per cent accuracy. The activity or severity of the arthritis cannot be correlated with the appearance of the chest film. The pulmonary lesions may precede the arthritis by several years, but in most cases the onset of arthritic symptoms and the development of the lung lesions coincide.—*An epidemiological study of rheumatoid arthritis associated with characteristic chest X-ray appearances in coal workers, W. E. Miall, A. Caplan, A. L. Cochrane, G. S. Kilpatrick, & P. D. Oldham, Brit. M. J., December 5, 1953, No. 4848:1231.*—(*E. A. Riley*)

Pneumonoconiosis.—Iron ore miners who had never been exposed to any other risk of pneumonoconiosis provided 400 chest roentgenograms for study. The lesions found in them were reticular, "pinhead," or micronodular. Extensive opacities of the pseudotumoral type were seen only exceptionally. Pneumonoconiosis of iron miners does not progress like silicosis (Author's summary).—*Images pulmonaires anormales chez les mineurs de fer du bassin de Lorraine, P. Simonin, J. Girard, P. Sadoul, J. Dechoux, & C. Mertz, Presse med., October 1, 1953, 61: 1227.*—(*V. Leites*)